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Review Article

THE IMPACT OF SGLT2 INHIBITORS AND GLP-1 RECEPTOR AGONISTS ON COGNITIVE OUTCOMES IN DIABETES: A SCOPING REVIEW

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ABSTRACT

Introduction: Diabetes is associated with accelerated cognitive decline and an elevated risk of dementia. While sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) are established glucose-lowering therapies with cardiovascular and kidney benefits, their effects on cognitive outcomes in people with diabetes remain uncertain

Objectives: The study aimed to synthesize the impact of SGLT2 inhibitors and GLP-1R as on cognitive outcomes in people with diabetes.

Methodology: A scoping review was conducted in accordance with PRISMA-ScR. Targeted searches were undertaken in PubMed and major publisher platforms (BMJ, JAMA Network, ScienceDirect) for English-language studies published from January 2010 to July 2025.

Results: SGLT2 inhibitors and GLP-1 receptor agonists were generally associated with **better cognitive outcomes and lower dementia risk** in people with type 2 diabetes, although most evidence came from **real-world cohort studies and target-trial emulations** rather than randomized trials. Across large population datasets, SGLT2 inhibitors showed **substantially lower dementia incidence** compared with DPP-4 inhibitors, including reductions in Alzheimer's disease and vascular dementia. Similarly, GLP-1 receptor agonist initiation in older adults was linked with **reduced dementia risk** compared with sulfonylureas and

DPP-4 inhibitors.

Conclusion: Findings suggest potential cognitive benefit or risk reduction for dementia with SGLT2 inhibitors and GLP-1RAs in people with diabetes. However, confounding by indication, heterogeneity of dementia ascertainment, and limited randomized cognitive endpoints restrict causal inference.

Keywords: diabetes; dementia; cognitive impairment; SGLT2 inhibitors; GLP-1 receptor agonists; scoping review

INTRODUCTION

Dementia and type 2 diabetes mellitus (T2DM) are among the most prevalent conditions with the most significant impacts on ageing populations. Diabetes-associated cognitive impairment falls within a spectrum between insidious impairment of attention, executive functioning, and psychomotor speed to mild cognitive impairment (MCI) and frankly diagnosed dementias. Impaired cognition may have a detrimental effect on diabetes self-management, raise the risk of medication errors and hypoglycaemia as well as loss of independence, caregiver burden and increased health-care utilization.

There is substantial epidemiologic evidence that diabetes patients are at increased risk of cognitive decline and dementia as compared to non-diabetics. In the exploratory cognitive analysis of the REWIND cardiovascular outcomes trial, researchers summarized the that indicated that persons with diabetes were about 1.5 to 2.0 times more prone to encounter cognitive deterioration, cognitive deficiency, or dementia (Cukierman-Yaffe et al., 2020). Systematic review and meta-analysis have also validated the relationship between diabetes and subsequent dementia in later life, which is overall indicative that long-term risk-factor modification might also apply to the health of the brain (Cukierman et al., 2005; Gudala et al., 2013). The mechanisms connecting diabetes to ageing of the brain are multifactorial and comprise chronic hyperglycaemia, insulin resistance and impaired central insulin signalling, cerebrovascular and microvascular damage, frequent hypoglycaemia, and inflammatory and oxidative stress, which may be combined with Alzheimer related and vascular pathology (Biessels & Despa, 2018).

Over a decade, the emergence of two classes of drugs: sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) redefine T2DM management. These agents in their syntheses have shown to be beneficial in terms of major adverse cardiovascular events, hospitalization due to heart failure, and progression of chronic kidney diseases in relevant populations (Palmer et al., 2021). Such pleiotropic actions have elicited increased interest in whether SGLT2 inhibitors and GLP-1RAs can also have an effect on cognitive paths, either via the indirect effects of ameliorating vascular and metabolic risk factors or via direct actions on central nervous system pathways.

SGLT2-inhibitors reduce plasma glucose through diminishing the reabsorption of glucose by the kidney and stimulating the re-excretion of glucose into the urine. In addition to glycaemic effects, they usually decrease body weight and blood pressure, and have a minimal inherent risk of hypoglycaemia when combined with neither insulin nor sulfonylureas. The connections between SGLT2 inhibition and cognitive

benefit are enhanced cerebral vascular health due to cardiometabolic risk modification, decreases in the systemic inflammation and oxidative stress, enhanced endothelial activities, and a metabolic shift to availability of ketone bodies that may serve as an alternative energy source in cerebral tissues in insulin-resistance states. But the question of whether these mechanisms do confer clinically significant cognitive benefits on diabetic individuals still remains uncertain and needs to be substantiated in research that has sound dementia ascertainment and longitudinal cognitive testing.

GLP-1RAs increase glucose-stimulated insulin release, decrease glucagon release, and increase satiety and loss of weight. In neurocognitive hypotheses, GLP-1 receptors are present in the learning and memory parts of the brain, and some GLP-1RAAs have the ability to penetrate the blood-brain barrier. According to preclinical models, GLP-1 signaling has the potential to suppress neuroinflammation and oxidative stress and can also regulate the amyloid-B and tau-related process, but its application to clinical outcomes is not well known yet. In humans, they are reflected in exploratory trial data that involves the use of cognitive outcomes, especially in REWIND, and an expanding pharmaco-epidemiologic literature on the incidence of dementia in users of GLP-1RA (Cukierman-Yaffe et al., 2020).

Although biologically plausible and with comprehensive programs of cardiometabolic trials, cognitive outcomes are not commonly endpoints of glucose-lowering trials, and even dementia outcome differs significantly between administrative claims and electronic health records data. The evidence base is thus heterogeneous and includes exploratory analyses of cardiovascular outcomes trials, cohort studies and more recent target trial emulation strategies meant to enhance the causal interpretability of observational comparisons. Comparator choice is also important in the interpretation of comparative effectiveness results since older therapies vary in multiple meaningful ways on hypoglycaemia, weight, and common prescribing indicators- factors that may confound an association between cognitive outcomes. Against this context, the scoping review proves to be highly appropriate to survey whatever has been researched, sum up direction and strength of reported associations, and determine gaps that ought to guide future randomized trials and rigorous real-world examinations on brain health in diabetes.

METHODOLOGY

Study design and reporting: This study was conducted as a scoping review to provide the scope of evidence rather than a single pooled effect. It was based on the methodological framework by Arksey and O'Malley (2005) and subsequent improvements that highlight the benefit of a transparent and iterative study selection and data charting (Levac et al., 2010). Reporting was designed based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension to Scoping Reviews (PRISMA-ScR) checklist (Tricco et al., 2018).

Inclusion criteria: We used a Population-Concept-Context structure to select peer-reviewed articles of human studies that included adults with diabetes (type 1 or type 2), assessed exposure to an SGLT2 inhibitor and/or a GLP-1 receptor agonist as a current therapy or an initiated therapy, reported at least one cognitive

outcome measure, such as incident all-cause dementia, Alzheimer's disease, vascular dementia, mild cognitive impairment, or longitudinal change of a standard. We omitted any preclinical studies, case reporting and those articles that lacked a defined comparator group. Articles that were written in English and those published since January 2010 to July 2025 were taken into consideration.

Sources and search strategy: Specific searches were done in PubMed/MEDLINE and in addition, searches were done of major publisher sites containing literature on diabetes outcomes (BMJ, JAMA Network, and ScienceDirect). The search concepts were diabetes; SGLT2 inhibitors including empagliflozin, dapagliflozin, and canagliflozin; GLP-1 receptor agonists such as dulaglutide, liraglutide, semaglutide, exenatide, and tirzepatide; and cognitive outcomes like dementia, Alzheimer, vascular dementia, cognitive impairment, and mild cognitive impairment. Included studies and similar reviews were screened to produce references lists that would generate extra eligible evidence.

Samples: The scoping review involved a sample of 9 studies. All articles were in English language and were published in peer reviewed journals. In total, there were 412 records that were obtained in the database and publisher-platform search. Following an elimination of 96 duplicates, 316 articles were screened by title and abstract; 274 were excluded at the first level of eligibility criteria, mostly because of being wrong on population/exposure/comparator/outcome or lack of primary human data. 42 full-text articles were evaluated on the basis of eligibility and 33 were excluded at full-text stage, mostly due to either being wrong on population/ exposure/ comparator/outcome or lack of primary human data. In total, the number of subjects represented in the studies included was ≥ 380,912.

Data Extraction: We have charted the setting, design, sample size, diabetes population, drug exposure and comparator, follow-up, outcome definition, and significant effect estimates, hazard ratios or relative risks with confidence intervals where possible, of each study that was included. The synthesis of evidence was in the form of a narrative of drug class and domain of outcomes. Since there is heterogeneity in the definitions of cognitive outcomes, and in the study design, no meta-analysis was done.

Critical appraisal: In line with scoping review methodology, the quality of the study was not applied to eliminate evidence. Nonetheless, we have recorded design characteristics that apply to internal validity in order to put in context the credibility of reported designs.

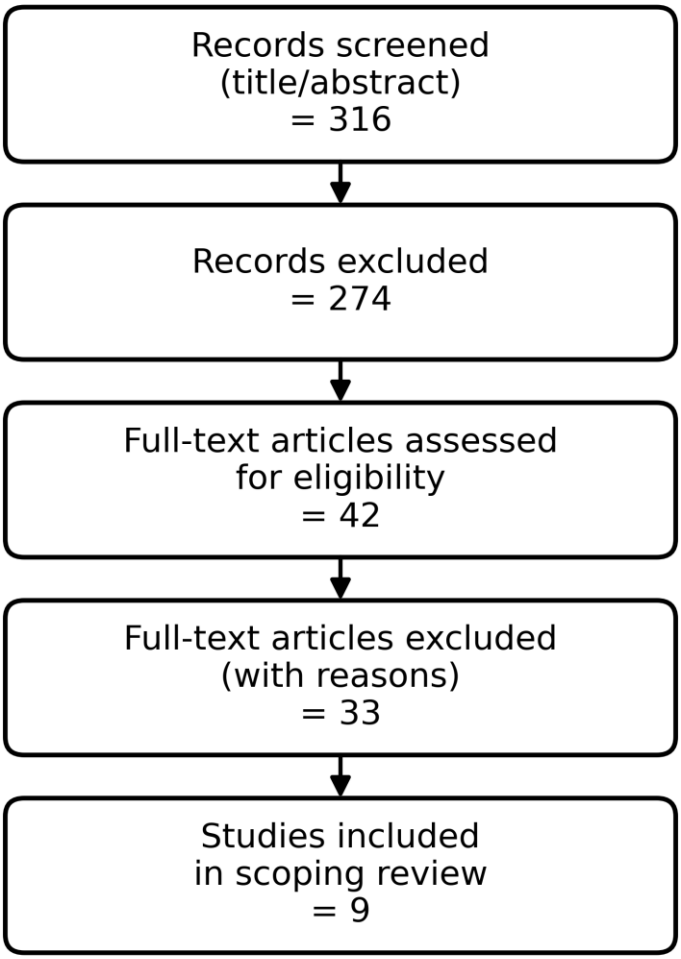

Figure 1: Flow diagram of literature review

RESULTS

Study selection and characteristics:

The literature included a combination of randomized trial outcomes, mostly exploratory cognitive analyses of cardiovascular outcome studies, trial emulations on a basis of linked national registers, and observational cohort studies on the basis of administrative claims or electronic health records. Cognitive outcomes were outlined in the majority of the studies as incident all-cause dementia defined by a diagnostic code and/or anti-dementia medication prescription, with less frequent studies using repeated standardized cognitive tests. Overall, active-comparator new-user designs using propensity-score techniques were typical of studies of higher quality, as a measure of the attempt to address confounding by indication.

Evidence base was greater on dementia incidence compared to longitudinal cognitive test performance. The studies were mainly about type 2 diabetes and most of them were done in high-income environments where the linkable health records were available including South Korea, Sweden, Canada, and multinational networks of electronic health records.

Study (setting)	Design / population	Exposure vs. comparator	Outcome(s)	Key findings
Shin et al., 2024 (South Korea)	Population-based cohort; 110,885 propensity-score matched pairs; adults 40–69 years with T2DM, no prior dementia; mean follow-up 670 days.	SGLT2 inhibitor initiators vs DPP-4 inhibitor initiators.	Incident dementia; dementia requiring drug treatment; Alzheimer's disease; vascular dementia.	Lower dementia incidence with SGLT2 inhibitors: 0.22 vs 0.35 per 100 person-years; HR 0.65 (95% CI 0.58–0.73). Lower risk also observed for dementia requiring drugs (HR 0.54), Alzheimer's disease (HR 0.61), and vascular dementia (HR 0.48).
Wu et al., 2023 (Ontario, Canada)	Population-based retrospective cohort; adults ≥66 years with T2DM initiating therapy 2016–2021.	New SGLT2 inhibitor use vs new DPP-4 inhibitor use.	Time to incident dementia (administrative data).	Study reported an association consistent with lower dementia risk among SGLT2 inhibitor initiators compared with DPP-4 inhibitor initiators; dementia outcomes were identified using health administrative data.
Tang et al., 2024 (Sweden)	Sequential trial emulation using national registers; n=88,381 adults ≥65 years with T2DM; mean follow-up 4.3 years.	GLP-1 agonist initiation vs DPP-4 inhibitor initiation vs sulfonylurea initiation.	Incident dementia.	GLP-1 agonists associated with lower dementia risk vs sulfonylureas (HR 0.69, 95% CI 0.60–0.79) and vs DPP-4 inhibitors (HR 0.77, 95% CI 0.68–0.88) in intention-to-treat analysis; stronger effects in per-protocol analyses.

Cukierman-Yaffe et al., 2020 (REWIND; multinational)	Randomized, double-blind, placebo-controlled trial (exploratory cognitive analysis); 9,901 randomized; 8,828 with baseline cognitive data; median follow-up ~5.4 years.	Dulaglutide vs placebo (added to standard care).	Composite cognitive impairment outcome based on standardized tests (MoCA and DSST components).	Unadjusted analysis: HR 0.93 (95% CI 0.85–1.02; p=0.11). After post-hoc adjustment for baseline cognitive scores: HR 0.86 (95% CI 0.79–0.95; p=0.0018), suggesting potential benefit but requiring confirmation in trials with prespecified cognitive endpoints.
Lin et al., 2025 (TriNetX, US network)	Retrospective cohort using electronic health records; 60,860 propensity-score matched adults ≥40 years with T2DM and obesity; follow-up up to 7 years.	Semaglutide or tirzepatide vs other antidiabetic drugs.	Incident dementia; ischemic stroke; intracerebral hemorrhage; Parkinson disease; all-cause mortality.	Lower dementia risk (HR 0.63, 95% CI 0.50–0.81), lower ischemic stroke risk (HR 0.81, 95% CI 0.70–0.93), and lower all-cause mortality (HR 0.70, 95% CI 0.63–0.78) among semaglutide/tirzepatide users.

Table 1: Key studies evaluating SGLT2 inhibitors and GLP-1 receptor agonists in relation to cognitive outcomes in diabetes

SGLT2 inhibitors and cognitive outcomes:

The strongest real-world signal for SGLT2 inhibitors and incident dementia risk comes from large active-comparator cohort studies using new-user designs., Over a mean follow-up of 670 days, 1,172 incident dementia cases were identified, and SGLT2 inhibitor initiation was associated with a lower risk of dementia (HR 0.65, 95% CI 0.58–0.73). Importantly, the association was observed for dementia requiring drug treatment (HR 0.54) and across dementia subtypes, including Alzheimer's disease (HR 0.61) and vascular dementia (HR 0.48), suggesting that both neurodegenerative and vascular pathways may be relevant (Shin et al., 2024).

The greatest real-world signal of SGLT2 inhibitors and incident risk dementia is provided by large active-comparator cohort designs using new-user designs. In a Korean National Health Insurance Service cohort of adults aged 40–69 years with T2DM, Shin et al. (2024) compared initiators of SGLT2 inhibitors with

initiators of DPP-4 inhibitors using propensity-score matching (110,885 pairs). A total of 1,172 incident dementia cases were found in a mean of 670 days, and the initiation of SGLT2 inhibitors was related to a reduced risk of developing dementia (HR 0.65, 95% CI 0.580.73). The correlation was found in dementia drug treatment (HR 0.54) and in the subtypes of dementia, such as the Alzheimer disease (HR 0.61) and the vascular dementia (HR 0.48), indicating that both vascular and neurodegenerative mechanisms might be involved (Shin et al., 2024).

The same BMJ research indicated that the benefit was more apparent as follow-up duration increased and was found to be generally similar across patient subgroups (sex, concomitant metformin use, and baseline cardiovascular risk) (Shin et al., 2024). Such findings are hypothesis-generating but they also pose critical questions of methodology. Specifically, observational comparisons can be prone to lag effects, informative censoring, different medication adherence, and changing clinical signals to initiate drug therapy.
The older populations evidence is provided by a population-based cohort study of Ontario residents aged 66 years and above who initiated the SGLT2 inhibitors or DPP-4 inhibitors (Wu et al., 2023). The study offers valuable additional evidence in a more aged, high-risks cohort, where dementia incidence is more prevalent and outcome is much more ascertained in administrative data.

In addition to these seminal cohorts, slightly smaller observational studies have investigated SGLT2 inhibitors in particular high-risk clinical scenarios such as atrial fibrillation, heart failure, and comorbid psychiatric conditions, in many cases applying concepts of target trial emulation including new-user cohorts and active comparators. These studies differ in the definition of dementia, their choice of comparators and the ability to control time-varying confounding, which does not directly compare them. Collectively, the existing evidence indicates that there may be a positive relationship between the use of SGLT2 inhibitors and the occurrence of dementia, but no trial with adjudicated cognitive functions has confirmed this.

Systematic reviews and meta-analyses have tried to use dementia research to summarize the SGLT2 inhibitor evidence base, yet a summary is limited by the preponderance of observational studies as well as poor capture of dementia events in randomized studies. As an example, a meta-analysis in Diabetes Therapy combined observational comparisons and reported the overall result of dementia incidence reduction in users of SGLT2 inhibitors, but the heterogeneity was also observed by baseline cardiovascular risks and comorbidity (Gunawan & Gunawan, 2024). These syntheses support the general pattern of associations but underline the necessity to standardize the definition of outcomes and pay attention to the biases related to time.

GLP-1 receptor agonists and cognitive outcomes:

GLP-1RAs bear a slightly larger body of evidence, which incorporates randomized cognitive tests and several large-scale real-world studies as compared to SGLT2 inhibitors. In REWIND, an exploratory cognitive outcome was integrated into a massive cardiovascular outcomes trial that is randomized. In the unadjusted analysis, dulaglutide had no significant effect in reducing the outcome of composite cognitive impairment relative to placebo (HR 0.93, 95% CI 0.85102; p=0.11) yet, the hazard ratio obtained was sensitive to the

post-hoc adjustment of baseline cognitive scores (HR 0.86, 95% CI 0.79095) (Cukierman-Yaffe et al., 2020). This trend highlights the potential of GLP-1RAs, as well as the drawbacks of basing, on the results of an exploratory analysis that was not specified as the primary endpoint.

The assessment of cognition in REWIND incorporated simple standardized tests, such as the Montreal Cognitive Assessment (MoCA), which was initially created as a screening test of mild cognitive impairment (Nasreddine et al., 2005).

Tang et al. (2024) conducted a Swedish sequential trial emulation that combined emulated trials of Swedish nationally registered participants with T2DM starting the initiation of GLP-1 agonists or DPP-4 or sulfonylureas (n=88,381). Initiation of GLP-1 agonists was also found to be lower risk relative to sulfonylureas (HR 0.69, 95% CI 0.600.79) and relative to DPP-4 inhibitors (HR 0.77, 95% CI 0.680.88). The effect was also greater in per-protocol analyses (HRs of about 0.41 compared to sulfonylureas and 0.38 compared to DPP-4 inhibitors), and this could indicate that sustained exposure can have a role to play in the event of a causal effect (Tang et al., 2024).

An analysis of EHRs has studied newer incretin-based therapies on scale. The authors utilized the TriNetX US network to compare adults with T2DM and obesity who started semaglutide or tirzepatide with those who started on other antidiabetic medications using propensity-score matching (30,430 matched pairs). Semaglutide or tirzepatide use was also linked to reduced risks of dementia (HR 0.63, 95% CI 0.500.81), ischemic stroke (HR 0.81, 95% CI 0.7095% CI 0.630.81), and all-cause mortality (HR 0.70, 95% CI 0.630.78) in seven year follow-up (Lin et al., 2025)

Through non-diabetes cohorts, there has been an increase in interest in incretin-based treatment of neurodegenerative outcomes. GLP-1RAs have been studied in a number of large programs on obesity and cardiometabolic outcomes, these trial platforms have spurred discussions regarding the inclusion of brain health endpoints in future studies (Jastreboff et al., 2022; Kosiborod et al., 2024). Although these trials are not a direct assessment of the prevention of dementia, they indicate that it is possible to conduct long-term randomized exposure to GLP-1 pathway therapies and that older populations are safe contexts.

Comparative effectiveness studies on tirzepatide and GLP-1RA that investigate broader clinical outcomes in T2DM also demonstrate rapid adoption and changing patterns of prescription that can affect observational studies of dementia (Chuang et al., 2024). According to GLP-1RA studies, the selection of comparators seems to affect the estimates of effects. The comparisons with sulfonylureas and insulin secretagogues can not only possibly embody the neuroprotective effects of GLP-1RA but also capture differences in risks of hypoglycaemia and weight gain of older agents. Indication sharing Active comparators sharing similar prescribing indications may minimize confounding by indication, but unaddressed confounding and misclassification of outcomes may persist across any observational design.

The results on dementia were more often than not based on regular clinical codes which could not establish milder forms of dementia and did not have standardized subtype adjudication. Follow-up periods were disparate and several cohorts had shorter mean follow-up than the prodromal period of dementia,

which increased the likelihood of reverse causality in the case of medications being prescribed to respond to early changes in functionality. Exposure definitions included intention-to-treat style analyses to as-treated analyses where discontinuation is censored which may cause informative censoring in case discontinuation is related to early cognitive decline or frailty.

There is little evidence of effects on cognitive test performance as opposed to incident dementia. The highest randomized evidence was offered by REWIND, based on standardized tests, and the cognitive outcomes were exploratory, and the observed advantage was found after post-hoc adjustment. Specific randomized studies employing prespecified cognitive outcomes and extended follow-up and adjudicated dementia outcomes are a significant gap.

DISCUSSION

The scoping review identified a rapidly evolving literature that explored the relationship between SGLT2 inhibitors and GLP-1 receptor agonists and cognitive outcomes in diabetes. In several observational cohorts and trial emulations, the initiation of either of the drug classes was typically related to a reduced incidence rates of incident dementia in comparison with active comparators. The strongest observational data regarding SGLT2 inhibitors include a large cohort of new users in Korea that reported the same risk reductions in all-cause dementia and dementia subtypes (Shin et al., 2024). In the case of GLP-1RA, the evidence of lower incidence of dementia was found in a real-world trial emulation in Sweden and electronic health record analysis in the United States (Tang et al., 2024; Lin et al., 2025). The evidence on randomized is relatively smaller: the REWIND cognitive analysis indicated the potential advantage of dulaglutide based on the post-adjustment analysis to baseline cognitive scores, whereas the unadjusted analysis did not reach statistical significance (Cukierman-Yaffe et al., 2020).

Cardiometabolic risk profile and vascular health improvements may be translated to reduced dementia rates especially vascular dementia. The association was numerically stronger in the Korean cohort with vascular dementia compared to the Alzheimer disease (Shin et al., 2024) in line with the hypothesis that interventions with ability to reduce the burden of microvascular injuries, blood pressure, and heart failure would selectively affect the vascular contribution to cognitive impairment and dementia. Meanwhile, the decrease in the number of Alzheimer diagnoses was also noted, which caused the suspicion that there might be common pathways or the potential diagnosis misclassification in general data.

Biological plausibility and mechanistic considerations:

The two classes of drugs have plausible mechanisms that may influence brain ageing which though have not been entirely proven to be central effects in humans. With regards to SGLT2 inhibitors, the potential neurocognitive pathways are enhanced glycaemic stability and reduced risk of hypoglycaemia, reduced systolic blood pressure and weight loss, and improvements in heart failure and kidney disease that are correlated with cerebrovascular risk. Experimental hypotheses also focused on availability of ketone bodies

and mitochondrial efficiency, which would be applicable to brain energy metabolism where there is insulin resistance. In the case of GLP-1RAs, GLP-1 receptor signaling in the central nervous system, anti-inflammatory effects, and possible modulation of synaptic plasticity have been suggested. Nevertheless, preclinical indications do not translate into clinical protection and the extent and length of exposure necessary to produce neuroprotection remains unknown.

These mechanisms are put in perspective by a number of recent syntheses and genetic epidemiology studies. The article has presented the possible potential of a more recent GLP-1RA called semaglutide in the context of neurodegenerative diseases, in addition to its metabolic actions (Mahapatra et al., 2022). Moreover, Mendelian randomization studies treating SGLT1/2 inhibition with genetic instruments have shown correlations with a reduced risk of neurodegenerative conditions, in support of the possibility of a causal relationship between these pathways and brain outcomes (Liu & Shi, 2024). This type of evidence is complementary to clinical pharmacoepidemiology, but in no way can substitute randomized cognitive endpoint trials.

Methodological limitations:

Causal interpretation is limited by a number of methodological problems. First, there is the widespread issue of confounding by indication: patients who are started on SGLT2 inhibitors or GLP-1RA can be systematically different in aspects that are not completely represented by administrative covariates. Propensity-score matching new-user active-comparator designs such as those applied by Shin et al. (2024), Tang et al. (2024), and Lin et al. (2025) minimize but not eliminate this bias. Second, diagnostic-code ascertainment of dementia can overlook milder disease, be vulnerable to health-care utilization patterns and usually inadequate high-fidelity subtype information. Third, early cognitive deterioration may cause early medication initiation, adherence or discontinuation, which is analogous to reverse causality but can be resolved by lag periods and sensitivity analysis; lag periods and sensitivity analyses cannot be applied in a consistent manner. Fourth, many cohorts, even with a follow-up, have shorter periods of follow-up compared to the prodromal period of dementia and this prevents differentiation between prevention and delayed diagnosis.

Implications for clinical practice:

Recent clinical guidelines suggest SGLT2 inhibitors and GLP-1RAs should be used to achieve glycaemic and cardiovascular-kidney risk benefits in the right groups of patients. According to the evidence on point, it is too early to recommend either of the classes of medication either to predict cognitive deterioration or dementia. However, even in patients with T2DM who already fulfil the criteria of such therapies i.e. a known cardiovascular disease, chronic kidney disease, or obesity, the new evidence indicates that there can be some side effects of benefit on the brain health. The clinicians are to consider the findings on observational dementia as supportive, but not conclusive, and they must still focus on the personal therapy selection criteria on cardiovascular-kidney risk, hypoglycaemia risk, tolerability, and patient preferences.

LIMITATIONS

The search strategy was focused on large biomedical databases and publishers platforms and might not have included all the potential eligible studies, especially those published in non-English language or those published in non-global journals that are not indexed in the searched sources. Due to the nature of this being a scoping review, we did not formally do any quantitative synthesis and we did not filter studies according to quality; hence conclusions need to be viewed as a map of the evidence landscape and not as a conclusive estimate of effect. Lastly, since the literature is changing at a fast rate, the balance of the evidence can shift further as the trials are still ongoing and new observational studies are being conducted.

CONCLUSION

In a diverse and increasingly emerging body of evidence, SGLT2 inhibitor and GLP-1 receptor agonist initiation has often been linked to reduced incidences of incident dementia in diabetes patients versus active comparators. In the case of SGLT2 inhibitors, the best evidence is provided by large new-user cohort studies that have shown the same associations across the dementia subtypes. In the case of GLP-1RAs, there is an indication of similar or stronger association with trial emulations and analysis of electronic health records, and exploratory randomized data are supportive, but not definitive. Currently, the facts are too few to define the causality or prescribe a particular drug group to the prevention of dementia. Further studies are needed to focus on specific trials, expert dementia adjudication, and powerful real-world emulations to know whether such therapies can significantly maintain cognition in diabetes.

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